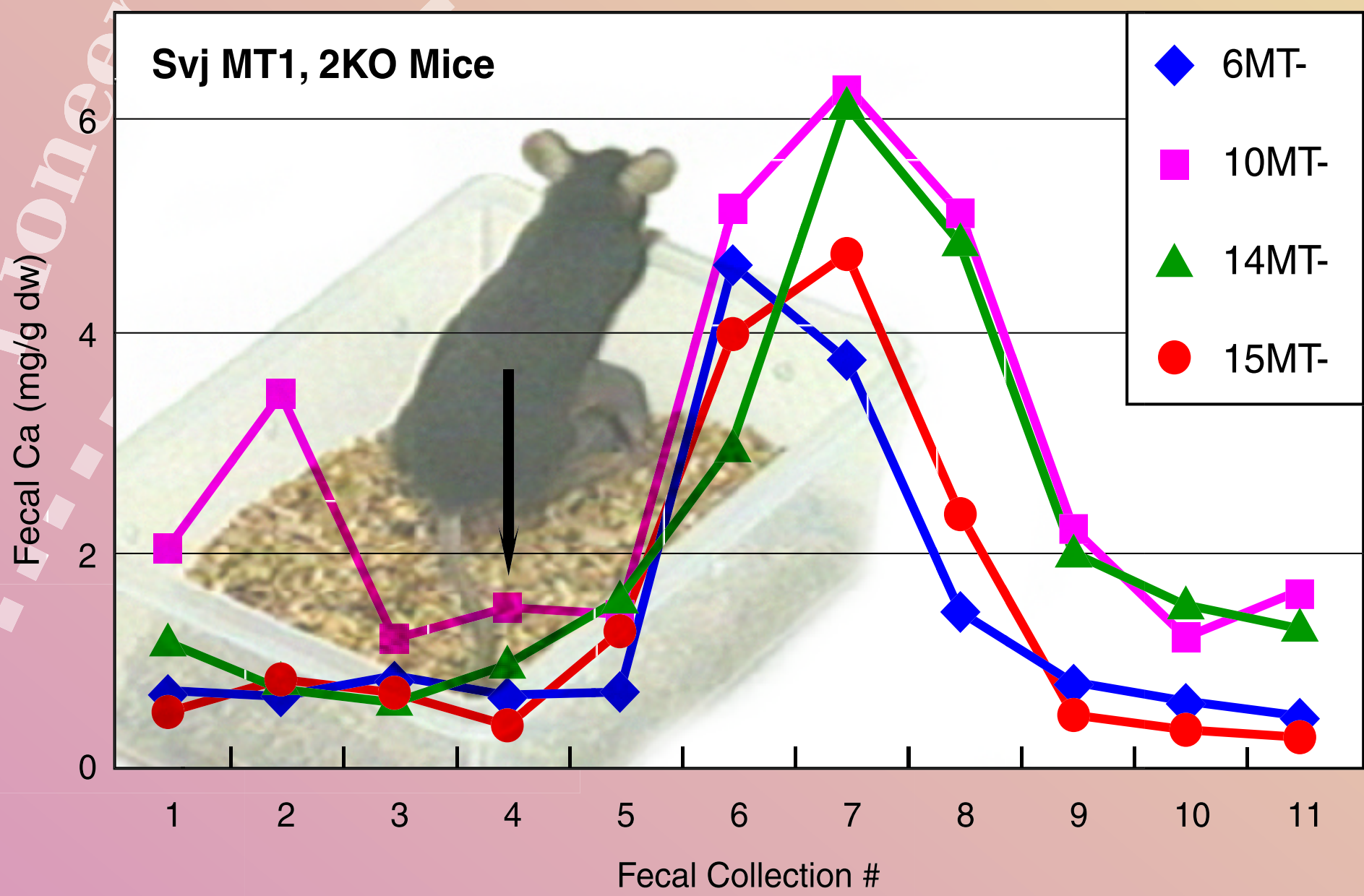


Sounding the Alarm About Bone Loss

Challenge

Osteoporosis threatens the health and independence of aging Americans. As people age, osteoporosis increases the chance of hip and other disabling bone fractures — particularly in post-menopausal women. Although its causes are still elusive, Argonne researchers have found that exposure to cadmium — found in many industrial environments and cigarettes — can accelerate bone loss.



Bone response to cadmium. Single oral cadmium dose, given at arrow above, caused transient increase in bone calcium excretion in mice feces. (Each line represents results from an individual mouse [total of four mice].)

Argonne's Findings

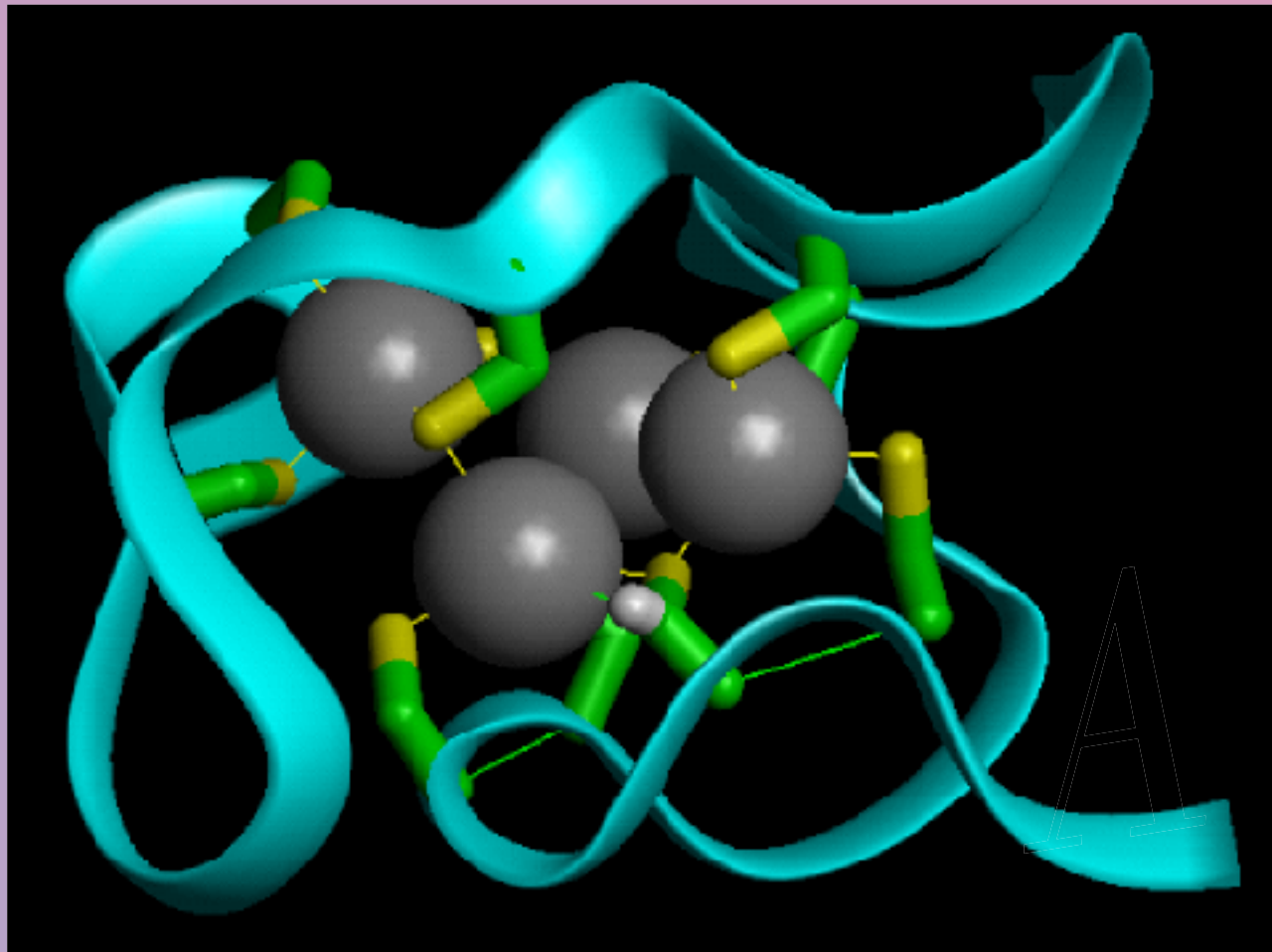
- In laboratory animals, bone loss begins almost immediately after exposure to cadmium — well before the onset of classical cadmium-related kidney damage and at blood concentrations below current OSHA standards for cadmium exposure.
- Exposure to cadmium — such as by smoking cigarettes — activates two types of gene expression pathways in bone cells early after exposure: (1) toxic-response pathways that stimulate bone loss and (2) protective pathways that counteract cadmium's toxic effects.
- An unknown gene is multiplied nearly 20-fold within four hours after cadmium exposure. Researchers plan to clone and sequence this gene to determine its role in the bone cell's response to cadmium.

Sponsors:

- National Institutes of Health
- U.S. Department of Energy, Office of Science

Collaborators:

- Benedictine University, Illinois
- Eastern Washington University, Washington



Cadmium causes the body to produce more metallothionein. This protein tightly binds cadmium in the cytoplasm, keeping it away from the bone cell's toxic response sites.

Argonne's Approach

Argonne researchers are investigating the cellular specifics of cadmium-related bone loss. Scientists are monitoring changes in protein and gene expression after an organism's exposure to cadmium. Through this research, scientists are learning more about the detailed response pathways in bone cells.

Cadmium Exposure Levels in Perspective

Group	Blood Cadmium Concentration*
Dogs (start of bone response)	2–5 µg/L
Nonsmokers	0.26 ± 0.03 µg/L
Smokers (≥ 20 cigarettes/day)	2.5 ± 1.5 µg/L
Battery plant workers	22 µg/L

*For comparison, the OSHA action level is 5 µg/L.

Observing which bone cell genes change in their expression after exposure to cadmium helps scientists find out how cadmium causes bone loss. RNA isolated from mouse bones 2 or 4 hours after exposure by ingestion was subjected to a microarray analysis that contained probes for about 8,500 mouse genes — nearly the entire mouse genome.

"The remarkable power of this approach is that we can query an organism's entire genome to devise one specific new hypothesis."

Maryka Bhattacharyya, principal researcher

